Exophthalmos

From the Standpoint of the Ophthalmologist

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• There are many causes of abnormal protrusion of one or both eyes, the most common of which is imbalance of the glands of internal secretion. Among other causes are a variety of tumors that originate behind the eye or that extend to that location from other parts in the body. Infections can extend to the orbit behind the eye from the neighboring structures such as the paranasal sinuses. Infection may also extend to the orbit from distant areas by way of the blood and cause exophthalmos.

DETERMINATION OF THE CAUSE and treatment of exophthalmos is one of the most difficult problems confronting ophthalmologists.

Because the orbit is essentially a closed vault, except for the eye, the cardinal symptom of retrobulbar, space-occupying lesions is proptosis. There are a great variety of benign and malignant tumors that may occur in the orbit. They can be best classified according to (1) the age of patients in whom they develop and (2) their position of growth and extension in relation to the muscle cone.

The primary orbital tumors of infancy and childhood include hemangiomas, gliomas of the optic nerve, dermoid tumors, teratomas and various benign and malignant tumors of mesenchymal origin.

Gliomas of the optic nerve obviously occur within the muscle cone and cause protrusion of the globe without lateral or vertical displacement. Such neoplasms arise from the glial cells of the optic nerve and/or from the cells of the nerve sheath. A glioma may arise as a fusiform thickening of the nerve within the orbit or the optic foramen, or within the prechiasmal portion of the nerve; and it may grow, usually slowly, posteriorly and anteriorly. Although gliomas usually are regarded histologically as benign, they are clinically malignant in that they may cause optic atrophy and consequent blindness and they may extend posteriorly to invade the brain. Gliomas also bring about enlargement of the optic foramen and distortions of the pituitary fossa that are discernible radiologically. Surgical removal by the intracranial route, unroofing the optic canal and/or orbit, with subsequent enucleation anteriorly, is the treatment of choice.

Hemangiomas occur in the same age group and within the muscle cone. They, too, may cause enlargement of the optic foramen. They permit compressibility of the globe and often extend sufficiently anteriorly so that their presence is indicated by discoloration. In young persons they are usually radiosensitive.

Various congenital tumors, including teratomas and dermoid tumors, while usually occurring as epibulbar masses, may grow retrobulbarly and cause exophthalmos. They arise outside the muscle cone and therefore may bring about lateral or vertical displacement of the globe. Dermoid tumors are often situated at orbital suture lines and often extend intracranially, a possibility that should always be kept in mind. X-ray films should be taken to determine the possible presence of bony dehiscence, and the ophthalmologist and neurosurgeon should collaborate in the surgical treatment.

Undifferentiated sarcomas of the orbit are among the most malignant neoplasms occurring in childhood. Their origin is obscure, their growth rapid, and they spread early and extensively. The least malignant of this group are rhabdomyosarcomas. Immediate exenteration followed by irradiation is the treatment usually considered best. Some observers, however, believe that irradiation effects temporary control by fibrosis and encapsulation. If it does, there is some basis for irradiation first, then excision.

There are numerous orbital tumors that occur in adults. Hemangiomas are common. They are unilateral, usually nonmalignant, are often encapsulated and may frequently produce intermittent exophthalmos that can be accentuated by jugular compression and dependent position. They may be confused with meningiomas because of their tendency to calcify and to cause hyperostosis of the orbit. They are often of the cavernous type, and although usually roentgen-sensitive, they may be resistant because of their intervascular fibrosis.

Meningiomas may arise from the optic nerve sheath or from the dural extension along the orbital

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walls, or they may invade the orbit from adjacent structures. They early produce papilledema and optic atrophy, often impair ocular motility and produce osteoplastic hyperostosis in most instances. While they are usually of the common spindle cell fibroblastic type, sarcomatous vascular forms do occur. Tumors of the latter group and the recently described *hemangiopericytoma* were previously often classified as endotheliomas.

Bony tumors of the orbit cause hyperostosis but are differentiated from meningiomas in that they usually appear in persons less than 20 years of age, whereas the hyperostosis of dural meningiomas does not appear in persons younger than 30.

Mixed tumors of the lacrimal gland obviously occur temporally outside the muscle cone and displace the globe inferiorly and nasally. They often cause decrease in the flow of tears, are locally recurrent and destroy bone. They are usually roentgen-resistant. They have been called mixed tumors because of great stromal as well as cellular change. It is now thought by many observers that only the cellular elements are significant and that the varied stromal changes merely reflect altered degrees and types of tissue reaction to parenchymal trauma.

The various lymphomas form a group of neoplasms that are ill-defined as to origin and are little understood as to prognosis. In contrast to lymphocytic lymphomas that occur as solitary, oval, subconjunctival masses anteriorly, and that are clinically benign, the retrobulbar lymphomata are of all types and may sometimes occur with or give rise to widespread, generalized malignant lymphomas. The differentiation between chronic inflammation, lymphoma, Mikulicz's disease, and "pseudotumor" is possibly a matter of degree rather than of kind. Bone marrow studies and survey of the reticuloendothelial system may establish the diagnosis of lymphoma. "Pseudotumor" is accompanied by pain and in many cases disappears temporarily with the systemic administration of cortisone. All tumors of this group are quite sensitive to x-ray.

Tumors originating in Schwann's sheath, such as neurofibromas of von Recklinghausen, neurinomas, neurilomas and melanomas may be primary in the orbit and produce exophthalmos. In addition there is a great variety of tumors that either extend to the orbit from neighboring structures or occur there by metastasis from distant origins. Such metastatic tumors are not uncommon. The possibility of their presence must be kept in mind and a diligent search made for them in every unexplained case of exophthalmos.

Acute inflammation of the orbit often causes forward displacement of the globe. The most common causes of inflammation are bacteremia, extension of infection from adjacent paranasal sinuses and the teeth, and penetrating and nonpenetrating injuries. These conditions may result in periostitis, osteomyelitis, subperiosteal abscess, occasionally in a true abscess of soft tissue, and at times in thrombophlebitis. Clinically such conditions are characterized by edema and redness of the lids, proptosis, limitation of motion, pain and tenderness, chemosis and induration of the subcutaneous tissues. Usually the signs and symptoms of severe systemic infection with characteristic changes in the blood and in body temperature are present. It is to be remembered that extraocular muscle paresis can acompany such processes. Extension of infection from the paranasal sinuses is the most common cause of this group of conditions.

Vascular abnormalities, congenital anomalies, trauma, infections or neoplastic processes may cause abnormal arteriovenous shunts, which in turn may cause pulsating exophthalmos, perhaps intermittent, often of variable degree. A thrill may be palpated; a bruit may be heard. The central retinal vein may or may not be distended and give evidence of decompensation. The episcleral and conjunctival vessels are usually distended and dilated. Because such lesions are often in the wall of the carotid sinus, extraocular muscle paresis is usually apparent. The vertical muscles are most frequently affected. Depending upon the degree and severity of involvement and the nature of the structures involved, this condition is classified as either the syndrome of the orbital apex or the syndrome of the cavernous sinus. Vascular abnormalities and accidents are, of course, more frequent in the latter category. When the clinical findings are not conclusive, angiography is perhaps indicated, although this diagnostic procedure is not without complications. Complete hemiparesis may result from injections of radiopaque material into the internal carotid artery. Often exploratory craniotomy becomes advisable. The author has observed four cases in which there was abnormal arteriovenous communication within the cranial vault at the apex of the orbit. Signs and symptoms were relieved by ligation of the involved vessels. Proptosis may be intermittent and may be influenced by dependent position and carotid compression. Carotid compression may influence the character of the bruit. Damage to the trigeminal nerve accompanied by disturbances in sensation is not uncommon.

There are numerous systemic lesions that will produce unilateral or bilateral exophthalmos. Disorders of fat metabolism, the so-called xanthomatoses, may do so. Localized xanthoma with deposition of cholesterol may occur within the orbit. More complicated abnormalities of conjugate fat metabolism such as Schuller-Christian disease may produce exophthalmos. It is possible to have localized angio-

neurotic edema, supposedly owing to allergic reaction, that will cause unilateral proptosis.

The most difficult problem concerning exophthalmos is that associated with endocrine dysfunction.

Bulging of eyelids with exophthalmos has been discussed by Rundle and Wilson,[2] who described the mechanism of exophthalmos and lid protrusion. They differentiated bulging from prolapsed fat and from edema. The variations in the plane of the eyelids, whether shrunken, normal or bulged, reflect corresponding variations in degree of orbital filling. The clinical characteristics of bulged lids are well defined and by considering them together with exophthalmometer readings it is possible to differentiate the particular pathologic process involved.

Rundle and Pochin[3] reported upon changes in orbital tissue that are associated with thyrotoxicosis. They concluded that the exophthalmos in Graves' disease is accounted for quantitatively by increase in the bulk of retrobulbar tissue. The increase is relatively greatest in the eye muscles, the fat content of which may be doubled in thyrotoxicosis. The changes are most pronounced in the levator of the lid. Smelser[4] noted that orbital fat contains connective tissue septa that absorb water in instances of thyrotropic exophthalmos. In experiments, when this orbital fat was transplanted elsewhere it still became unduly hydrated in the thyrotropic state. Conversely, fat lower in content of fibrous tissue that was transplanted to the orbit did not invite excessive water to that site and did not produce exophthalmos in experimentally produced thyrotropic states.

Mulvany,[1] in an excellent discussion of exophthalmos, considers two major classifications of the disease: thyrotoxic and thyrotropic. In thyrotoxic exophthalmos, as Mulvany describes it, the orbital contents are normal except for the extraocular muscles, which are pale, thinned and atrophic and show a patchy discoloration caused by an increased amount of interfascicular fat. Exophthalmos, more apparent than real in this condition, results from the retraction of the lid secondary to overstimulation of Mueller's muscle which is innervated by the sympathetic system. Mulvany describes thyrotropic exophthalmos, in which there is an excess of thyrotropic hormone in the serum, as characterized by enlargement of the individual extraocular muscles. This increase in size is accompanied by alteration of color and consistency. The muscles become pale and grayish and their soft structure becomes hardened and rubbery. This change is attributed to fibrosis and edema secondary to lymph stasis. There is inflammatory infiltration by lymphocytes and plasma cells. The pathological process involves the lacrimal gland and nerves. The actual amount of orbital fat may be decreased. The degenerative processes adequately explain the permanent muscle paresis that is often present.

In the author's experience, the division between the thyrotropic and thyrotoxic state is variable and indistinct. Often patients show varying degrees of both syndromes. The problem then is most difficult and at times requires consultation of internist, ophthalmologist and neurosurgeon.

Too often treatment becomes symptomatic and is directed toward the various complications that may arise. Recession of the levator muscles is often necessary to protect the cornea. Suturing of the lids may be extremely difficult. Despite the efforts of the internist and the ophthalmologist, decompression of the orbit may be advisable.

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